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Simultaneous estimation of finasteride and tamsulosin hydrochloride by reverse phase HPLC in bulk and pharmaceutical dosage form

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Abstract
This investigation describes a new simple, precise, sensitive and accurate RP-HPLC method for the Simultaneous estimation of Finasteride and Tamsulosin Hydrochloride in Bulk and Tablets. The resolution of two drugs was achieved on Symmetry C_{18} (150mm x 4.6mm i.d., 5µm particle size) column with UV detection at 245 nm and the mobile phase consist of Buffer and Acetonitrile and Water (15:75:10v/v).Using chromatographic conditions described Finasteride and Tamsulosin Hydrochloride were well resolved with mean retention times of 2.325 and 4.296 min, respectively. Linear response (r>0.999) was observed over the range of 62-312µg/mL for Finasteride and 5-25µg/mL for Tamsulosin Hydrochloride. The lower limit of quantification and lower limit of detection was 9.95 and 2.95 for Finasteride and 9.91and 2.97 for Tamsulosin Hydrochloride. The Validation parameters were performed according to the ICH guidelines and the proposed method can be useful in the routine analysis for the determination of Finasteride and Tamsulosin Hydrochloride in Pharmaceutical dosage forms.

Key-Words: Finasteride, Tamsulosin Hydrochloride, HPLC, Symmetry column, Validation parameters

Introduction
Finasteride (FINA) is a synthetic 4-azasteroid compound with the chemical name of azaandrost-1-ene-17-carboxamide,N-(1,1-dimethylethyl)-3-oxo-,(5α,17β).Tamsulosin Hydrochloride (TAMS) is an antagonist of alpha1A adrenoceptors in the prostate and chemically described as (-)-(R)-5-[2-[[2-(o-Ethoxyphenoxy)ethyl]amino]propyl]-2-methoxybenzenesulfonamide, monohydrochloride. Both drugs in combination used in the treatment of Benign Prostatic Hyperplasia, Enlarged Prostate. According to the literature survey it was found that few analytical methods such as Visible, UV, HPLC, HPTLC were reported for FINA and TAMS individually and with the other drug combinations In this communication, a new simple, rapid and precise HPLC method have been reported for simultaneous determination of FINA and TAMS which can be used for its routine analysis in normal laboratories.

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Material and Methods
Chromatograms were made on Waters (Alliance) with Auto Sampler and Ultraviolet detector. The data acquisition was performed by Empower Software. Glass wares used in each step were rinsed thoroughly with double distilled water, dried in hot air oven. FINA and TAMS were obtained from pharma train institution and Alekhya drugs. The pharmaceutical preparation of combination of Finasteride and Tamsulosin Hydrochloride is Urimax F (Cipla Ltd. India.). Acetonitrile used is HPLC grade obtained from MERCK (India) and water used is double distilled water. Other reagents were of AR grade.

Chromatographic conditions
The used analytical column was Symmetry C_{18} (150mm x 4.6mm i.d., 5µm particle size) column. The mobile phase consists of mixture of Buffer and Acetonitrile and Water (15:75:10v/v), filtered through 0.45µm Millipore filter and degassed by sonication. Separation was carried out isocratically, at ambient temperature (23±1°C), and a flow rate of 0.8 mL/min with Ultraviolet detection at 245nm.The injection volume was 20 µl.

Preparation of standard solutions

Accurately weigh and transfer 10 mg of FINA and 10 mg TAMS into a 100mL clean dry volumetric flask separately. Add about 70mL of Diluent (Mobile phase) and sonicate to dissolve completely and make volume up to the mark with the same solvent (Stock solution).Further pipette 18.7ml & 1.5ml of FINA and TAMS from the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent.

Analysis of marketed formulation

Twenty tablets of FINA and TAMS were crushed and made into powder. Accurately weigh and transfer equivalent to15 mg of sample into a 100mL clean dry volumetric flask. Add about 70mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution).From the above stock solution, 3.7ml of FINA and TAMS was transferred into a 10ml volumetric flask and dilute up to the mark with diluent.20 µL of the standard, sample were injected into the chromatographic system and the areas were measured for the FINA and TAMS peaks. The content of FINA and TAMS were calculated and found to be 99.9% and 99.7% respectively.

Results and Discussion

Optimization of Chromatographic Conditions

Chromatographic conditions were optimized by changing the mobile phase composition and buffers used in the mobile phase. Different experiments were performed to optimize the mobile phase, but adequate separation of drugs could not be achieved. By altering the pH of mobile phase a good separation was achieved. The optimized mobile phase consisting of 0.05 M Potassium dihydrogen Phosphate (pH 6.5 with Sodium hydroxide), Acetonitrile and water mixed in the ratio of 15:75:10v/v and flow rate of 0.8 ml/min, FINA and TAMS were eluted at 2.325 and 4.296 minutes respectively with a run time of 7 min, under the above optimized chromatographic conditions. Typical chromatograms for simultaneous estimation of FINA and TAMS had shown in Figure 1 and 2.

Method validation

System Suitability Results

For FINA and TAMS peaks the tailing factor were found to be 1.6 &1.4 respectively and the

Theoretical Plates obtained were found to be 2373.9 & 3500.0 respectively.

Linearity

The calibration curves were obtained by plotting Peak Area against Concentration for FINA and TAMS. The linearity was obtained in the concentration range of 62-312µg/mL for FINA and 5-25µg/mL for TAMS. The regression coefficient values (R^2) for FINA and TAMS were found to be 0.999 respectively.

Accuracy and precision

The accuracy of the RP-HPLC method was determined by calculating Recoveries of FINA and TAMS for 50%, 100% and 150% with respect to target concentration and results are tabulated in Table 1 & 2 respectively. The System precision of the proposed method was determined by injecting standard solution for five times and measured the area for them in HPLC. The Method Precision of the proposed method was determined by injecting six sample solutions into HPLC prepared individually. The %RSD for the areas of system precision and method precision data were calculated and given in Table 3.

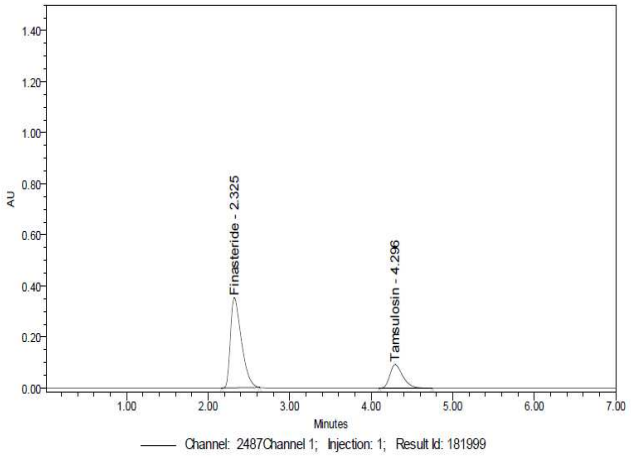

Fig. 1: Chromatogram of FINA and TAMS Standard

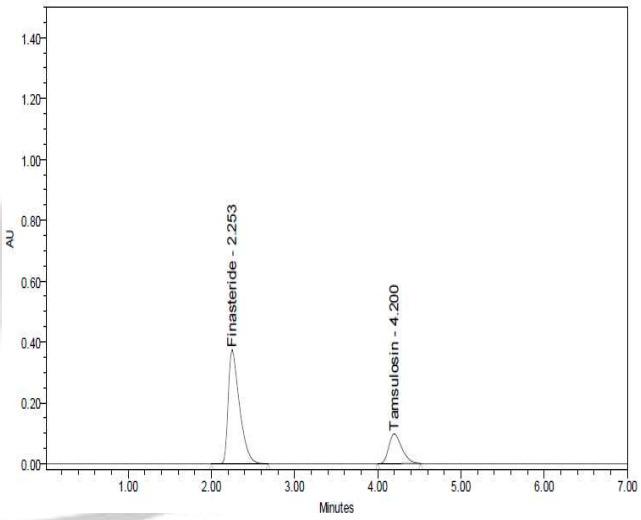

Fig. 2: Chromatogram of FINA and TAMS Sample

Table 1: Recovery Results for FINA

%Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	1829739	5.0	4.95	99.0%	99.1%
100%	3642243	10.0	9.85	98.5%	
150%	5535371	15.0	14.9	100.4%	

Table 2: Recovery Results for TAMS

%Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	564367	5.0	5.03	100.7%	100.1%
100%	1115445	10.0	9.95	99.5%	
150%	1682465	15.0	15.0	100.1%	

*Milligram

Table 3: Precision of FINA and TAMS

Precision	FINA	TAMS
System precision (Average Area and %R.S.D)	3347025and 0.90	1023985and 0.2
method precision (Average Area and %R.S.D)	3640925 and 0.56	1057121 and 0.16

Limits of Detection and Quantitation

For determining the limit of detection (LOD), 10mg of FINA and TAMS was transferred in 100 mL clean dry volumetric flask separately. Add about 70mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution) separately. From this a working standard of 0.06µg/mL and0.02 µg/mL of FINA and TAMS was prepared and injected separately. The LOD was found to be 2.95 for FINA and 2.97 for TAMS

For determining the limit of Quantitation, from the above stock solution, prepared 0.02µg/mL solution of FINA and 0.06µg/mL solution of TAMS and injected. The LOQ was found to be 9.95 for FINA and 9.91 for TAMS respectively.

Robustness

Robustness, a deliberate change in the flow rate, mobile phase composition was made to evaluate the impact on the method. The results reveal that the method is robust enough. The results are summarized in Table 4, 5, 6 and 7.

A new HPLC method was developed and validated for simultaneous determination of FINA and TAMS in combined pharmaceutical dosage form and assured the satisfactory precision and accuracy and also determining lower concentration of each drug in its solid dosage form. The method has been found to be better apart from few methods are reported, because of use of a less economical and readily available mobile phase, lack of extraction procedures, no internal standard and use of the same mobile phase for washing of the column. All these factors make this method suitable for quantification of FINA and TAMS in bulk drugs and in pharmaceutical dosage forms. It can therefore be concluded that use of the method can save much time and money and it can be used in small laboratories with very high accuracy and a wide linear range.

Table 4: System Suitability results for FINA (Flow Rate Varied)

S/No	Flow Rate (mL/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1.	0.7	2299.9	1.7
2.	0.8	2329.4	1.6
3.	0.9	2181.5	1.7

Table 5: System Suitability results for TAMS (Flow Rate Varied)

S/No	Flow Rate (mL/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1.	0.7	3325.9	1.4
2.	0.8	3498.4	1.4
3.	0.9	3156.1	1.4

Table 6: System Suitability results for FINA (Mobile Phase Varied)

S/No	Change in Organic Composition in the Mobile Phase	System Suitability Results	
		USP Plate Count	USP Tailing
1.	1.0% less	2314.3	1.5
2.	*Actual	2329.4	1.6
3.	1.0% more	2199.8	1.5

Table 7: System Suitability results for TAMS (Mobile Phase Varied)

S.No	Change in Organic Composition in the Mobile Phase	System Suitability Results	
		USP Plate Count	USP Tailing
1	1.0% less	3315.9	1.4
2	*Actual	3498.5	1.4
3	1.0% more	2872.7	1.3

***** Results form actual Mobile phase composition (Buffer and Acetonitrile and water (15:75:10v/v) have been considered from Accuracy standard

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